REMARKS

Claims 1-10, 24-40, 42-43, 49-60, 62-75 are pending. Claims 11-23, 41, 44-48 and 61 have been withdrawn from consideration and have been canceled as shown above, without prejudice or disclaimer. Applicants reserve the right to file a continuing application directed to the subject matter of the canceled claims at any time during the pendency of this application

Claims 1-10, 24-43, 49-60, 62-66, 74 and 74 stand variously rejected under 35 U.S.C. §§ 112, first paragraph, enablement and second paragraph. The Examiner has maintained the enablement rejection and the provisional double patenting rejection. In addition, a new rejection under 35 U.S.C. § 112, first paragraph, written description was set forth in the Office Action.

Claims 1 and 67-69 have been amended herein to correct typographical errors. In particular, a typographical error in claim 1 has been corrected. Applicants note that the error appeared only in the body of the previous response and that both the version showing changes made and the currently pending claim set did not contain this typo. Claims 1 and 2 have also been amended to make explicit what was previously implicit in the term "expression cassette," namely that the polynucleotide sequence is operably linked to a promoter. (See, page 24, line 22 to page 25, line 2). Further, claims 67-69 have been amended as suggested by the Examiner to replace "a polynucleotide..." with "the polynucleotide." No new matter has been added as a result of these amendments and entry thereof is respectfully requested. The amendments are made to expedite prosecution and are not made for reasons related to patentability.

In view of the following remarks and foregoing amendments, Applicants respectfully request reconsideration of the application.

Sequence Listing

A revised sequence listing is submitted herewith. Therefore, Applicants have fully complied with the requirements of 37 C.F.R. 1.821-1.825.

IDS

Applicants acknowledge with appreciation that the references submitted with Paper No. 19 have been considered.

Specification

The specification was objected to for containing an embedded hyperlink. Applicants have removed the hyperlink by amendment herein, thereby obviating this rejection.

35 U.S.C. 112, First Paragraph, Written Description

Claims 1-10, 24-43, 49-60 and 62-66 stand rejected as allegedly not described in the specification as filed in such a way as to reasonably convey to the skilled artisan that applicants were in possession of the claimed invention. (Office Action, page 3). In support of this rejection, the Office states:

> The claims recite a structure (polynucleotide encoding an immunogenic HIV Gag polypeptide) but do not recite a function for the genus of polynucleotide sequences. In addition, in view of the phrase "HIV Gag polypeptide", the polypeptide has to be identical to one found in an HIV in nature. The specification does not disclose how to distinguish between natural amino acid sequence and non-natural sequence that is also at least 90% identical. ...
>
> It is not sufficient to support the present claimed invention directed to a genus of a polynucleotide sequence encoding a polypeptide including an immunogenic HIV Gag polypeptide, wherein the polynucleotide sequence encoding said Gag polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO:1-4. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of polynucleotide sequences that must posses the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather it is an attempt to preempt the future before it has arrived [citing *Fiers* and *UC Regents v. Eli Lilly*]. ... The skilled artisan cannot envision the detailed structure of a genus of a polynucleotide encoding a polypeptide including an immunogenic HIV Gag polypeptide, wherein the polynucleotide sequence encoding said Gag polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO:1-4 that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. (Office Action, pages 5-6).

Because it is neither legally nor factually correct to assert that the skilled artisan could not envision the detailed structure of the claimed expression cassettes, Applicants traverse the rejection and supporting remarks.

The fundamental factual inquiry in written description is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. *See, e.g., Vas-Cath, Inc.*, 935 F.2d at 1563-64, 19 USPQ2d at 1117. Determining whether the written description requirement is satisfied is a question of fact and the burden is on the Examiner to provide evidence as to why a

skilled artisan would not have recognized that the applicant was in possession of claimed invention at the time of filing. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim*, 191 USPQ 90 (CCPA 1976). It is not necessary that the application describe the claimed invention *in ipsis verba*. Rather, all that is required is that the specification reasonably convey possession of the invention. *See, e.g., In re Lukach*, 169 USPQ 795, 796 (CCPA 1971). Finally, determining whether the written description requirement is satisfied requires reading the disclosure in light of the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lange*, 209 USPQ 288 (CCPA 1981).

As previously noted, the Patent Office's own guidelines on written description are clear -- the written description requirement is highly fact-dependent and there is a strong presumption that an adequate written description of the claimed invention is present at the time of filing:

> [t]he description need only describe in detail that which is new or not conventional. This is equally true whether the claimed invention is a product or a process. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that the applicant was in possession of the claimed invention, i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such characteristics. ...
>
> A "representative number of species" means that the species that are adequately described are representative of the entire genus. ... What constitutes a "representative number" is an inverse function of the skill and knowledge of the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. ... Description of a representative number of species does not require the description be of such specificity that it would provide individual support for each species that the genus embraces. (Final Examiner Guidelines on Written Description, 66 Fed. Reg. 1099, emphasis added).

Simply put, there is absolutely **no** requirement that Applicants exemplify (or reduce to practice) every sequence falling within the scope of the claims in order to adequately describe the expression cassettes as claimed. Rather, the test is whether the specification contains sufficient disclosure regarding structural and functional characteristics of the claimed sequences to satisfy the written description requirement. In the pending case, the specification as filed more than adequately describes and details structure and function of the claimed polynucleotides.

The Scope of the Claims

Because any written description inquiry must begin with claim construction, it is important to note at the outset of this discussion that the claims clearly recite both the structure (sequence) and the function (encode an immunogenic HIV Gag polypeptide) of the recited polynucleotides. Indeed, the claims do not, as asserted in the Office Action, recite only structural characteristics. In addition to exhibiting the claimed sequence identity, the claimed polynucleotides must also encode an immunogenic HIV Gag polypeptide. Therefore, when properly construed, it is plain that only polynucleotide sequences having the recited structure and function are encompassed by the pending claims.

Applicants also traverse the Office's assertion that the specification requires that the polypeptide encoded by the claimed expression cassettes be "identical" to a naturally occurring Gag polypeptide. (See, Office Action, page 5). As noted above, the pending claims are all directed to synthetic polynucleotide (not amino acid) sequences having the requisite similarity to SEQ ID NO:1-4 and that encode any immunogenic HIV Gag polypeptide. Thus, the polypeptides encoded by the claimed synthetic polynucleotides must encode an immunogenic Gag polypeptide. It is clear from the specification as filed that the written description requirement is met with respect the claimed molecules.

The Specification Describes the Claimed Subject Matter

For the reasons of record and those discussed herein, the specification as filed fully describes the claimed subject matter. The specification describes, in detail, how Gag polypeptides are identified, for example by Western blotting, ELISA or the like and how to determine immunogenicity. (See, *e.g.*, Section 2.1.3, Examples 2 and 3). Further, sequences of various Gag-encoding polynucleotides (as well as Gag polypeptides themselves) were known at the time of filing and are described, for example, in the Background section and references cited therein. In fact, the specification clearly describes how to determine percent identity as between polynucleotides or polypeptides, for example in the text beginning on line 3 of page 17. Performing such alignments was routine and conventional. Any polynucleotide exhibiting the requisite 90% identity could then be readily tested for immunogenicity as described, for instance, in Examples 4-7 of the specification a filed.

It is axiomatic that the specification need only describe in detail that which is new or not conventional. (See, Guidelines on Written Description, page 275). In the case at hand, a skilled artisan reading the specification would have known that Applicants were in possession of claimed polynucleotides as recited in the claims in view of the specification's extensive disclosure of (1) precise sequences falling in the scope of the claims; (2) conventional, known methods of aligning polynucleotides; (3) conventional, known methods of expressing

polynucleotides; and (3) conventional, known methods of testing the expressed polypeptides for immunogenicity. In view of disclosure of the specification and state of the art, it would have been plain to the skilled artisan that Applicants were in possession of the claimed invention at the time the specification was filed.

Turning now to the Office's assertion that there are insufficient representative species described in the specification to adequately describe the alleged "broad genus" of polynucleotides, Applicants note that a "representative number" does not mean that each and every species falling within the genus must be disclosed. (See, Guidelines on Written Description, reproduced in part above). In the pending case, at least **six** representative species are described. (SEQ ID NOs:1-4, 20 and 21). For the reasons noted above, it is well within the purview of the skilled artisan, in view of the teachings of the specification, to align polynucleotide sequences and determine those having the requisite similarity to the sequences set forth in the claims. (See, *e.g.*, pages 17-19 and Examples). Accordingly, the representative number of species disclosed in the specification more than adequately convey to the skilled artisan that Applicants were in possession of the precisely claimed molecules at the time the application was filed.

The Cases Cited are Not Applicable

Furthermore, the Office's reliance of *Fiers v. Revel* and *Regents of the Univ. Calif. v. Eli Lilly* is misplaced. The written description requirement of section 112 is highly fact dependent and the claims, disclosure and state of the art in *Fiers* and *Eli Lilly* are entirely different from those in the case at hand. Indeed, the issue in *Fiers* or *Eli Lilly* was not whether these specifications disclosed a sufficient number of representative examples, but whether these specifications disclosed any structure at all. In fact, the application in these cases were completely devoid of any representative structural (sequence) examples. In contrast, Applicants' specification, as filed, and pending claims contain and recite specific sequences (structure) and functional characteristics.

Furthermore, the Federal Circuit's holdings in *Fiers* or *Eli Lilly* in no way necessitate that the claims be limited in scope to those sequences disclosed in SEQ ID Nos. Indeed, in *Fiers v. Revel*, the Federal Circuit indicated that, although disclosure of a method of isolating DNA did not adequately describe the DNA, the DNA itself may be properly defined by one or more of the following parameters: "structure, formula, chemical name or physical properties." Thus, it is possible that DNA can be entirely described by its physical properties, *i.e.* by function. Again, Applicants' disclosure and claims include both structure and physical properties and, accordingly, the cases cited by the Office are not relevant to case at hand.

Dr. Donnelly's Rule 132 Declaration Has Not Been Properly Considered

Applicants further submit that the Rule 132 Declaration of Dr. John Donnelly submitted with the last response has not been adequately considered as it relates to written description. In this regard, the Examiner asserts that because Dr. Donnelly focused on enablement the Declaration somehow "evidences":

> [that] a representative number of species of the claimed genus of polynucleotide sequences were not disclosed in the specification in such as a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, to make and use a genus of claimed polynucleotide sequences without an undue amount of experimentation. (Office Action, paragraph bridging pages 12-13).

In addition to confusing the written description and enablement requirements, this statement totally misconstrues and mischaracterizes Dr. Donnelly's declaration. At the time Dr. Donnelly prepared his Declaration, there was no written description rejection and, as such, there is no discussion specifically addressing whether there are a sufficient number of representative species to satisfy this requirement. Furthermore, Dr. Donnelly's declaration in no way suggests that a representative number of species were not disclosed. Instead, Dr. Donnelly sets forth facts regarding what the specification discloses. These facts are applicable to both written description and enablement. In particular, Dr. Donnelly establishes the following:

First, at the time the specification was filed, it was well known how to align polynucleotide sequences to determine percent identity. (See, Donnelly Declaration, ¶ 7).

Second, the specification teaches how to test any sequence falling within the claimed identity for its ability to express immunogenic HIV Gag polypeptides. (Donnelly Declaration, ¶¶ 8-9).

Third, the specification describes and aligns such sequences. (Donnelly Declaration, ¶ 7).

Using these and other facts, the declaration of record establishes that a skilled artisan would have recognized that Applicants were in possession of sequences having 90% identity to SEQ ID NO:1-4 and which encode an immunogenic HIV Gag polypeptide. The evidence in this regard includes the teachings of the specification, references cited in the specification, as well as the general state of the art at the time of filing. This convincing, factual evidence has been improperly ignored by the Office (*see, e.g., In re Alton*, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996)). Indeed, by misinterpreting the Declaratory evidence provided by Applicants and asserting that the affidavit is inapplicable to a written description inquiry, the Examiner is substituting personal knowledge for that of Dr. Donnelly. When a rejection is based on facts within the personal knowledge of the Examiner, the data relied upon should be stated as

specifically as possible, and the reference must be supported, when called for by the applicant, by an affidavit from the Examiner. 37 C.F.R. 1.104(d)(2); MPEP 2144.03. Applicants respectfully request such an affidavit.

In view of the foregoing, Applicants submit that the pending claims are fully described by the specification as filed and respectfully request that the rejection be withdrawn.

35 U.S.C. 112, First Paragraph, Enablement

Claims 1-10, 24-43, 49-60, 62-66, 74 and 75 remain rejected under 35 U.S.C. 112, first paragraph as allegedly not enabled by the specification as filed. It is acknowledged that the specification enables expression cassettes in which the polynucleotide is operably linked to a promoter. (Office Action, page 9). However, it is alleged that the specification does not enable sequences having 90% identity to SEQ ID NO:1-4 or the inclusion of such sequences in non-plasmid vectors. The Office Action further cites Ngo et al. (1994) in support of the position that the immunogenic function is unpredictable. (See, Office Action, page 9). In further support, the Office also cites *Genentech v. Novo Nordisk* and *Enzo v. Calgene*. (See, Office Action, page 11). The previously submitted Rule 132 Declaration was not addressed with regard to enablement.

Applicants traverse the rejection and supporting remarks.

Undue experimentation is not required to practice the claimed invention because the claims are enabled throughout their scope and, in addition, that the reference cited by the Examiner does not in any way establish unpredictability. Moreover, the Examiner has improperly ignored declaratory evidence establishing that the disclosure, as filed, enabled the claimed invention. When the *Wands* factors are considered, it is clear that the specification as filed fully enables the pending claims throughout their scope.

The Examiner has asserted that the claims encompass a large genus and that a representative number of species of that genus are neither contemplated nor taught in the specification. (Office Action, page 11). This is not a correct application of the law and, moreover, completely refuted by the evidence of record. Applicants are under no legal obligation to teach each and every member of a claimed genus. Rather, for a claimed genus, representative examples together with a statement applicable to the genus as whole is sufficient to establish enablement if the skilled artisan would expect the claimed genus could be used in the manner set forth. *See. e.g.*, U.S. Patent and Trademark Office's Training Materials on Enablement, p. 29. The present record is replete with representative examples and statements applicable to the genus as a whole.

Six representative examples of sequences falling within the scope of the claims are provided in the specification. (SEQ ID NOs:1-4, 20 and 21). Further, these representative examples are specifically recited in the pending claims, which, as acknowledged by the Office,

are separately patentable. In addition to these representative examples, statements applicable to the genus as whole are provided throughout the specification, for example, on page 17 *et seq.* where it is noted how to determine sequences falling within the requisite percent identity. At the time of filing, determining sequence identity was utterly routine. The specification also provides guidance (*e.g.,* Example 1 of the specification) regarding selection and modification of native Gag HIV sequences. Substantial guidance is also given in regards to determining whether a Gag polypeptide is expressed from the claimed expression cassettes and whether this polypeptide is immunogenic, as required by the claims. (See, *e.g.,* Examples 2-7 and Section 2.1.3, particularly page 30). Thus, the specification provides ample guidance as to identification, generation, and testing of expression cassettes that can be used in the claimed invention.

With regard to the Office's position that only plasmid delivery vehicles are enabled by the specification, Applicants again direct the Examiner's attention to Section 2.3.1 (pages 51-61), which contains extensive guidance on the use of non-plasmid gene delivery vehicles. In addition, Dr. Donnelly presented evidence directly relevant to this issue in his Declaration, namely Exhibit C (Durrani et al.) that describes the use of a plant virus to deliver HIV encoding sequences. Viral vectors have long been used to deliver HIV-encoding sequences and, in view of the teachings of the specification, it would certainly not require undue experimentation to use non-plasmid delivery vectors to deliver the claimed expression cassettes. (See, also additional Abstracts and publications attached hereto, including Paoletti and Schnell).

The Cited Reference Does Not Establish Unpredictability

The Examiner has cited Ngo et al. (1994) as allegedly establishing the unpredictability of the art as relevant to the claimed invention. Specifically, the Office Action reasserts that Ngo demonstrates that it would require undue experimentation to determine which molecules exhibiting 90% identity to SEQ ID NO:1-4 were immunogenic. (Office Action, page 9). However, upon careful review, it is clear that this reference is not relevant to the claimed subject matter.

The Examiner's position regarding Ngo appears to be that because there may be sequences that exhibit the requisite homology but are not immunogenic Gag polypeptides (for example because the tertiary structure of the polypeptide they encode is not predictable), undue experimentation would be required to make and use the claimed expression cassettes. (Office Action, page 9). This reasoning is entirely improper. Sequences that do not produce immunogenic Gag polypeptides are not encompassed by the claims. Further, it is well settled that time-consuming or expensive experimentation is **not** undue if it is routine. (See, *e.g.,* PTO Training Manual on Enablement, pages 30-31, citing *United States v. Telectonics Inc.,* USPQ2d 1217, 1223 (Fed. Cir. 1988), *cert. denied* 490 U.S. 1046 (1989) holding the disclosure of a single

exemplified embodiment and a method to determine other embodiments was enabling, even in the face of evidence that determining additional embodiments might require 6-12 months of effort and cost over $50,000). In the case at hand, the specification discloses six exemplified embodiments and methods of determining others. Dr. Donnelly's Declaration establishes that the methods of determining other embodiments (determining sequences falling within the claimed homology, expressing these sequences and testing them for immunogenicity) were completely routine at the time of filing. Thus, the possibility of generating inoperative embodiments allegedly established by Ngo is not relevant to the claimed invention. Moreover, the specification and the Donnelly Declaration effectively rebut any argument that making and using the claimed molecules requires undue experimentation.

The question of enablement is what the specification teaches one of skill in the art. In this case, the specification teaches one of skill in the art how to make and use the precisely claimed invention. (see, *e.g.,* Donnelly Declaration). Indeed, Applicants have repeatedly pointed to specific disclosures (including working examples and post-filing date evidence) that establish enablement. In addition, the supporting declaratory evidence of record clearly refutes any contention that the claims are not enabled.

The Cases Cited are Not Applicable

Finally, the Office asserts that the facts and holdings of *Genentech v. NovoNordisk* and *Enzo v. Calgene* are applicable to the pending application, allegedly because Applicants provide no more than a "plan or invitation." (Office Action, page 11). Neither *Genentech* nor *Enzo* is applicable to the facts of the pending application. In *Genentech*, the Federal Circuit held that the specification failed to describe the sequence of a specific material to be cleaved. The court also found that continued lack of success in producing the claimed proteins was further evidence of non-enablement. In stark contrast, the specification at issue discloses specific sequences of at least six species. Thus, unlike *Genentech*, Applicants are not claiming compositions in which the sequence and function are not disclosed. Like *Genentech*, the claims at issue in *Enzo* contained no structural limitations whatsoever -- they were defined solely in terms of function. In the pending case, the claims specifically recite both structure and function. As such, there is simply no attempt to "bootstrap a vague statement of a problem into an enabling disclosure," and the cases cited by the Office are not germane to the instant enablement inquiry.

The Declaration Evidence Has Not been Properly Considered

It is well established that declaratory evidence must be considered. *In re Alton,* 37 USPQ2d 1578 (Fed. Cir. 1996). In *In re Alton,* The Court of Appeals for the Federal Circuit held that it was error for the Examiner to dismiss, with conclusory statements, not only factual

statements but also statements of opinion presented in Declarations made by qualified persons of ordinary skill in the art. The Federal Circuit also commented that they were "aware of no reason why opinion evidence relating to a fact issue should not be considered by an Examiner." 37 USPQ2d 1578 at 1583 n10. Applicants have provided ample factual evidence that demonstrates that the specification as filed describes the subject matter of the pending claims. The Office in the pending case has failed to adequately consider and rebut the facts and reasoned conclusions presented in the Donnelly Declaration. When properly considered, the Declaration clearly establishes that the claimed polynucleotides are both enabled by and described in the specification as filed. The Declaration sets forth certain factual evidence upon which Dr. Donnelly bases a reasoned opinion.

Further, when Dr. Donnelly analyzed whether the sequences having at least 90% identity to SEQ ID NO:1-4 were enabled, he concluded:

> 5. It is my opinion that, as a technical matter, a skilled worker could have readily made and used the compositions and methods of the pending claims in light of the specification, together with the common general knowledge, tools and methods available in December 1999. I base this opinion on the facts set forth below; however, I call attention to the fact that it was considered routine experimentation at the time of filing to determine a sequence having (i) at least 90% sequence identity to SEQ ID NO:1-4 and (ii) encoding an immunogenic Gag polypeptide; to express such polynucleotides in stem cells or their progenitors; to deliver in a variety of ways such polynucleotides to generate an immune response in a subject. In addition, in drawing my conclusions, I have considered the nature of the claims, the quantity of experimentation required to practice the subject matter of the claims, the existence of working examples, the direction present in the specification, the state of the field at the time the application was filed and the level of skill in the art. ...
>
> 7. In December 1999, the quantity of experimentation required to identify sequences exhibiting 90% identity to SEQ ID NOs:1-4 was quite low. For example, BLAST software programs were commonly known and readily available on the Internet at this time. This set of programs allows for an easy alignment and determination of percent identity as between any sequences. The skilled worker could have easily used the BLAST or any number of other similar programs to determine the percent identity between sequences (in this case between any given sequence and those presented SEQ ID NOs:1-4). The specification also provides extensive guidance in this regard, for example, on page 17, line 3 through page 19. Working examples are also provided, for example comparisons of the claimed sequences to wild-type HIV sequences. (See, Figure 5). Furthermore, the skilled worker could have readily generated any sequence falling within the scope of the claims using routine methods, for example by utilizing PCR to generate sequences, by introducing point mutations and the like. Thus, it is my opinion that it would have required only routine

experimentation to determine sequences falling within the 90% identity, as claimed.

8. In addition, the specification provides significant direction for evaluating whether sequences having 90% identity to SEQ ID NO:1-4 encode an immunogenic Gag polypeptide. Those of us working in the field of gene delivery and immunology are well versed in the various tests for determining immunogenicity, which include computer analysis of sequences, comparison to known immunogenic sequences as well as functional tests (*e.g.*, ELISAs, CTL assays and others described in the Examples of the specification). Examples present in the specification demonstrate the generation of sequences and immunogenicity testing of these sequences. (See, Examples 1 and 4).

9. Furthermore, the state of the art in December 1999 was quite sophisticated with regard to determining both sequence identity and evaluating immunogenicity. I have described above some of the tools, programs and methods available in the field of recombinant nucleic acid technology in December 1999 and many other examples of homologous nucleic acid molecules that encode immunogenic proteins were also available. Therefore, it is my opinion that, following the guidance of the specification, a scientist could have readily made and used polynucleotide sequences that exhibit at least 90% sequence identity to SEQ ID NO:1-4 and which encode an immunogenic HIV Gag polypeptide.

10. Preparing polynucleotides encoding immunogenic Gag polypeptides in December 1999 was a predictable art. There is no doubt that a skilled worker would have been able to make and use sequences exhibiting 90% identity to SEQ ID NO:1-4 and encoding an immunogenic polypeptide. Even if a rare construct were inoperable for some reason (*e.g.*, it wasn't immunogenic), the skilled worker would have readily modified the construct according to the alternatives available at the time and described in the specification. In other words, to the skilled worker, an inoperable construct would itself be a useful starting material for other operable constructs. Essentially all molecules that fall within the claims would be useful for making or using defining technical features of the claims, *i.e.*, nucleotide sequences having 90% sequence identity to SEQ ID NO:1-4 and which encoded an immunogenic HIV Gag polypeptide.

Thus, using specific facts, Dr. Donnelly concludes that practicing the claimed invention does not require undue experimentation. This convincing, factual evidence has been improperly ignored by the Office (*see, e.g., In re Alton*, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996).

In sum, when the *Wands* factors are considered, it is clear that the record establishes that the specification as filed fully enables the pending claims throughout their scope. Therefore, Applicants submit that this rejection should be withdrawn.

Provisional Double Patenting

Applicants request the provisional double patenting rejection be held in abeyance until indication as at allowable claims is received in one of the applications.

CONCLUSION

In view of the foregoing amendments, Applicants submit that the claims are now in condition for allowance and request early notification to that effect.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §1.16, §1.17, and §1.21, which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648, referencing Atty. Docket No. 2302-1631.

If there are any remaining issues to be addressed before this case proceeds to issuance, Applicants request that the Examiner contact the undersigned at (650) 493-3400 in order to schedule a personal interview.

Please direct all further written communications regarding this application to:

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Respectfully submitted,

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